5. (amended) The method of claim 4, further comprising administering to the patient an effective amount of a further drug substance being effective in the treatment of rheumatoid arthritis.

Please add new claims 12-15 as follows:

-- 12. The method of claim 4, wherein the CD25 binding molecule further comprises a second domain which comprises in sequence, the hypervariable regions CDR1', CDR2' and CDR3', the CDR1' having the amino acid sequence Ser-Ala-Ser-Ser-Ser-Ile-Ser-Tyr-Met-Gln (SEQ ID NO: 4), the CDR2' having the amino acid sequence Asp-Thr-Ser-Lys-Leu-Ala-Ser (SEQ ID NO: 5) and the CDR3' having the amino acid sequence His-Gln-Arg-Ser-Ser-Tyr-Thr (SEQ ID NO: 6). --

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-- 13. The method of claim 12, wherein the first domain is part of an immunoglobulin heavy chain or fragment thereof and the second domain is part of an immunoglobulin light chain or fragment thereof. --

-- 14. The method of claim 4, wherein the CD25 binding molecule is a chimeric anti-CD25 antibody. --

-- 15. The method of claim 4, wherein the CD25 binding molecule is a single chain binding molecule. --

REMARKS

Favorable consideration of this application is respectfully requested in view of the foregoing amendment and the following remarks.

Claims 1-6 and 8-11 are pending. Claims 1-3, 6 and 9-11 have been cancelled without prejudice. Claims 4, 5 and 8 have been rejected. Claims 4 and 5 have been amended. New claims 12-15 have been added. Support for the language in new claims 12-15 can be found in the specification, e.g., at pages 2 and 3. No new matter has been added.

I. The Rejection of Claims 4, 5 and 8 Under 35 U.S.C. §112, Second Paragraph, May Properly Be Withdrawn.

With respect to this rejection, the Examiner contends that claims 4 and 5 depend from non-elected claim 1. In response to this rejection, claim 4 has been amended to incorporate the features set forth for the CD25 binding molecule of claim 1 and claim 5 has been amended to depend from claim 4.

In view of the above, withdrawal of the rejection of claims 4, 5 and 8 under 35 U.S.C. §112, second paragraph, is respectfully requested.

II. The Rejection of Claims 4, 5 and 8 Under 35 U.S.C. §112, First Paragraph, May Properly Be Withdrawn.

With respect to this rejection, the Examiner contends that there is insufficient written description of a CD25 binding molecule other than basiliximab. In particular, the Examiner states that the specification discloses that CD25 binding molecule means "any molecule capable of binding to the CD25 antigen either alone or associated with other molecules to form high affinity IL-2 receptors". The Examiner indicates that such a definition encompasses a large genus, and that the specification in exemplifying only basiliximab, does not includes a representative number of species to describe the claimed genus.

Applicants respectfully disagree with the Examiner's conclusion and submit that the specification contains sufficient written description of a CD25 binding molecule as set forth in amended independent claim 4 for the reasons stated below.

While "CD25 binding molecule" is defined in the specification as indicated above, the method of treatment defined in amended independent claim 4 does not encompass administering the large genus of CD25 binding molecule to a patient as asserted by the Examiner. Instead, the method of treatment defined in amended independent claim 4 encompasses administering a subgenus of "CD25 binding molecule" having specific features. The subgenus of "CD25 binding molecule" as recited in amended independent claim 4 comprises at least one antigen binding site comprising three hypervariable CDR regions, each CDR region defined by specific amino acid sequences. These CDR sequences are the key features of the CD25 binding molecule recited in amended independent claim 4 since these are the sequences responsible for specifically binding to the CD25 antigen. One skilled in the art reading the specification would recognize that a number of species of the CD25 binding molecule recited in amended claim 4 possess these specific CDR hypervariable regions, e.g., a monoclonal antibody, a chimeric antibody, e.g., a human/murine monoclonal antibody as exemplifed by basiliximab, a humanized antibody or fragments of the aforementioned antibodies. Accordingly, the specification discloses a representative number of species to describe the specific CD25 binding molecule as recited in amended independent claim 4.

In view of the above, withdrawal of the rejection of claims 4, 5 and 8 under 35 U.S.C. §112, first paragraph, is respectfully requested.

III. The Rejection of Claims 4, 5 and 8 Under 35 U.S.C. §103(a) May Properly Be Withdrawn.

With respect to this rejection, the Examiner contends that claims 4, 5 and 8 are unpatentable over WO 89/09622 (WO '622) in view of Kovarik et al. In particular, the Examiner states:

> "It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to perform a method of treating rheumatoid arthritis comprising administering an effective amount of a CD25 binding molecule, with or without coadministration of a further substance effective in the treatment of rheumatoid arthritis, as taught by WO 89/09622, employing basiliximab, as taught by Kovarik et al. One of ordinary skill in the art at the time the invention was made would have been motivated to use basiliximab as the CD25 binding agent because basiliximab was a well-known CD25 binding agent and was known that serum concentrations of basiliximab sufficient to saturate IL-2 receptors were achievable, as taught by Kovarik et al. Note that the saturation of IL-2 receptors is the mechanism by which the treatment of the instant claims would be expected to function."

Applicants submit that amended independent claim 4 is unobvious over the combination of cited references for the reasons stated below.

WO '622 describes anti-TAC chimeric antibodies. WO '622 further describes a long list of possible diseases, one of them being rheumatoid arthritis, that may be treated with the anti-TAC chimeric antibodies. As acknowledged by the Examiner, WO '622 does not teach or suggest a CD25 antibody comprising the hypervariable regions, CDR1, CDR2, CDR3 having the specific amino acid sequences as recited in amended independent claim 4. Additionally, WO '622 does not teach or suggest that the specific antibodies recited in amended independent claim 4 can be utilized to treat rheumatoid arthritis.

Kovarik et al. teach the specific chimeric monoclonal antibody, basiliximab, and the use of this antibody for immunoprophylaxis against acute rejection in renal transplantation. While Kovarik et al. indicate that serum concentrations of basiliximab sufficient to saturate IL-2 receptors were achieved, there is no teaching or suggestion in Kovarik et al. that binding of basiliximab to IL-2 receptor at serum concentrations sufficient to saturate the receptor to treat transplant rejection would also be effective to treat rheumatoid arthritis. Accordingly, Kovarik et al. does not remedy deficiencies present in WO '622.

In summary, Kovarik et al. is concerned only with immunoprophylaxis against rejection in renal transplantation and suggest nothing to a skilled person in the art about any possible utility of basiliximab in treating any other condition or disease. WO '622 describes a completely different antibody, anti-TAC, and mentions rheumatoid arthritis as a long list of possible diseases which could be treated by the anti-TAC antibody. It would therefore not have been obvious to a skilled person to combine these separate references and arrive at the subject matter of amended independent claim 4.

Applicants further assert that even if the references were combined, one skilled in the art would not have been motivated to utilize basiliximab to treat arthritis. With regard to this point, the Examiner states "one of ordinary skill in the art at the time the invention was made would have been motivated to use basiliximab as the CD25 binding agent, because basiliximab was a well-known CD25 binding agent and it was known that serum concentrations of basiliximab sufficient to saturate IL-2 receptors were achieved as taught by Kovarik et al. "

In support of Applicants' assertion of the lack of motivation by one skilled in the art to utilize basiliximab to treat arthritis, there is no teaching or suggestion in the references combined that the serum concentrations necessary to saturate the IL-2 receptor to suppress transplant rejections would also be effective to treat rheumatoid arthritis.

Additionally, no guidance is provided in the combined prior art that would lead one skilled in the art to pick and choose rheumatoid arthritis out of the long list of diseases recited in WO'622, as the specific disease that can be treated with basiliximab, other than hindsight knowledge of Applicants' invention. In this regard, it is duly noted that the Court has repeatedly cautioned against employing hindsight by using the Applicants' disclosure as a blueprint to reconstruct the claimed invention out of isolated teachings from the prior art. *Grain Processing Corp. v American Maize-Products Co.*, 840 F.2d 902, 5 U.S.P.Q. 2d 1788 (Fed Cir. 1988).

Further, while both transplant rejection and rheumatoid arthritis are associated with immunological factors, rheumatoid arthritis is considered a multifactorial disease associated with other factors besides immunological factors including psychological, hormonal, environmental and genetic factors. See Sany, *Rev. Rhum.*, Eng. Ed, pp. 197-205 (1993), cited in IDS. Thus, the presence of a multitude of factors that contribute to the etiology of rheumatoid arthritis would make an assessment of a positive clinical response to any untested agent complicated and difficult to predict. Further, one skilled in the art knowing that factors other than immunological factors are involved in the etiology of rheumatoid arthritis would not be able to reasonably predict that "serum concentrations of basiliximab sufficient to saturate IL-2 receptors" to treat transplant rejection would also be effective to treat rheumatoid arthritis.

Moreover, the references combined are devoid of any teaching or suggestion on dosing regimens, route of administration or duration of treatment with anti-TAC antibody or basiliximab that would be beneficial to ameliorate symptoms of rheumatoid arthritis. Indeed, no experimental data is provided in WO '622 which assesses the efficacy of administering anti-TAC antibody to treat rheumatoid arthritis, let alone basiliximab. Thus, for the reasons provided above one skilled in the art having knowledge of the cited prior art would not have been motivated to utilize basiliximab for the treatment of rheumatoid arthritis.

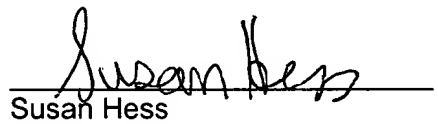
Accordingly, even if the references are combined they do not make obvious the claimed subject matter as defined in amended independent claim 4.

In view of the above, withdrawal of the rejection of claims 4, 5 and 8 under 35 U.S.C. §103(a) is respectfully requested.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned **"Marked-Up Version of the Changes Made"**.

A good faith effort has been made to place the present application in condition for allowance. If the Examiner believes a telephone conference would be of value, he is requested to call the undersigned at the number listed below.

Respectfully submitted,



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Date: February 4, 2003

Marked-Up Version of the Changes Made

IN THE CLAIMS:

Claims 1-3, 6 and 9-11 have been cancelled without prejudice.

Claims 4 and 5 have been amended as follows:

4. (amended) A method for the treatment of rheumatoid arthritis [or inflammatory or hyperproliferative skin diseases] in a patient in need of such treatment comprising administering to the patient an effective amount of a CD25 binding molecule [according to claim 1], wherein the CD25 binding molecule comprises at least one antigen binding site comprising at least one domain which comprises in sequence, the hypervariable regions CDR1, CDR2 and CDR3; the CDR1 having the amino acid sequence Arg-Tyr-Trp-Met-His (SEQ ID NO: 1), the CDR2 having the amino acid sequence Ala-Ile-Tyr-Pro-Gly-Asn-Ser-Asp-Thr-Ser-Tyr-Asn-Gln-Lys-Phe-Glu-Gly (SEQ ID NO: 2), and the CDR3 having the amino acid sequence Asp-Tyr-Gly-Tyr-Tyr-Phe-Asp-Phe (SEQ ID NO: 3).

5. (amended) [A method for the treatment of rheumatoid arthritis or inflammatory or hyperproliferative skin diseases in a subject in need of such treatment]The method of claim 4, further comprising administering to [said subject] the patient an effective amount of [a) a CD25 binding molecule according to claim 1 and b)] a further drug substance being effective in the treatment of rheumatoid arthritis [or inflammatory or hyperproliferative skin diseases].